REMARKS

Claims 1-27 are pending and stand rejected. In view of the discussion below, it is believed that all claims are patentable and that this application is now in condition for allowance.

Summary of the Invention of the Present Application:

The invention of the present application provides a composition and method for determining compliance with a medication regimen. This composition and method is rapid, simple, and inexpensive. In one embodiment, it includes an orally administrable composition in combination with at least one visual marker. This marker is present in a form and amount sufficient to cause a coloration of at least a portion of a mucous membrane or buccal membrane of the oral and/or pharyngeal cavity of a patient. Upon ingestion, the marker stains these membranes, and in certain embodiments, is designed to dissipate prior to ingestion of the next dose of medication. In various embodiments of the invention, by way of non-invasive observation of this coloration of the mucous or buccal membranes of the oral and/or pharyngeal cavity, one may obtain information regarding patient compliance with a medication regimen, such as whether the medication has been taken, the time elapsed since the medication was last taken, whether it is time for another dose of medication, etc. Thus, the present invention is very rapid, simple, and non-invasive as opposed to more invasive, tedious, and complicated monitoring methods of the prior art, such as the analysis of urine and

stool samples, and injection, implantation, or application of compositions, such as to cutaneous or subcutaneous tissues.

Claim Rejections 35 U.S.C. §112:

In the Office Action dated September 12, 2003, the Examiner rejected claims 1-27 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In that same Office Action, the Examiner had rejected claims 1-17, also under 35 U.S.C. §§102 and 103. More specifically, with respect to the rejection under §112, the Examiner stated that the phrase "contact staining" was new matter. In response, Applicants argued that a "contact staining" is inherent in the disclosure of the present application. However, in order to overcome the rejection, Applicants amended claims 1, 4, 5, 10-15, 19, and 24-27 to replace the phrase "contact staining" with the phrase "contact coloration."

In an Advisory Action issued on November 21, 2003, the Examiner stated that the proposed amendments would be entered. However, the Examiner maintained the rejection of claims 1-27. In the statement of the grounds for rejection attached to the Advisory Action, the Examiner stated that claims 1-27 would be maintained because the amendments did not overcome the cited prior art stated in the rejections under 35 U.S.C. §§102 and 103. In view of this statement, Applicants assume that the amendments that were entered did resolve the issue under 35 U.S.C. §112, first paragraph, and that that rejection has been withdrawn by the Examiner.

Claim Rejections 35 U.S.C. §102:

The Examiner has rejected claims 15-20 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,303,102 (the Schlichte '102 patent). In particular, regarding claim 15, the Examiner states that the Schlichte '102 patent discloses a marker in combination with one or more treatment drugs, medicaments, or a composition applied topically or orally, wherein the marker is a pigment or dye providing visual evidence for gauging the application and time since the application of the medicine. Applicants respectfully disagree with the rejection.

Regarding the Schlichte '102 patent, Applicants first note that the entire patent is directed only to use in coloration of, and observation in, cutaneous or subcutaneous tissues. (See at least the title, "Cutaneously Applied..."; column 2, lines 19-20, "What is lacking...is a cutaneously applied ... composition"; column 2, lines 33-34, "The instant invention provides a ... composition which is applied cutaneously or subcutaneously"; column 5, lines 16-19, "the pigment vehicle carries a colored pigment or dye suitable for administration into the dermis, or subcutaneous tissue, e.g. the fatty layer underlying the dermis"; and column 14, line 28, "applied cutaneously.") In contrast, Applicants submit that independent claim 15 of the present application recites the marker as causing contact coloration of a mucous or buccal membrane of the oral and/or pharyngeal cavity. Applicants further submit that the mucous and buccal membranes of the oral and/or pharyngeal cavity cannot be classified as cutaneous or

subcutaneous tissues. The cutaneous and subcutaneous tissues make up the tissues of and relating to the skin. The mucous and buccal membranes recited in the claims of the present application, on the other hand, are mucous-secreting membranes that line the oral and/or pharyngeal cavity. These membranes and tissues are wholly different substances.

The Schlichte '102 reference teaches marking of such cutaneous or subcutaneous tissue primarily through injection, such as into the cutaneous or subcutaneous tissue. For example, the reference teaches that an inoculation could mark the underside of a hide, the hide itself (cutaneous) or the fat at the injection site. Another alternative is an implant(subcutaneous). A process involving injection of a marker (or implantation of a marker) is completely different from the contact coloration described in the present application and recited in the claims. Injection is invasive. Injection requires the passage of some amount of time for the marker to appear. These are some of the very drawbacks that are discussed in the "Background of the Invention" section of the present application, and which the invention of the present application overcomes. A system involving injection or implantation is not suitable for a medication regimen as described in the present application due to the drawbacks described above and discussed in the present application.

By contrast, the invention of the present application overcomes all the drawbacks associated with injection and implantation (and with markers designed to

appear in cutaneous or subcutaneous tissues, as described in Schlichte), by providing and claiming an orally ingestable composition that colors the mucous or buccal membrane of the oral or pharyngeal cavity upon contact therewith. Such a method is simple and noninvasive. In contrast, nowhere is there a teaching or even a hint in the Schlichte '102 reference regarding a marker which is active for coloring a portion of a mucous membrane or buccal membrane of the oral/pharyngeal cavity. In fact, nowhere in the Schlichte '102 reference do the words "membrane" or "membranes" even appear.

However, in the Office Action dated September 12, 2003 and in the recent Advisory Action dated November 21, 2003, the Examiner has stated and maintained that the Schlichte reference discloses a marker in combination with a composition which may be applied orally, wherein the marker provides visual evidence of application and time elapsed since application. In response, Applicants first note that the Examiner does not state that the Schlichte marker colors a membrane of the oral and/or pharyngeal cavity, as is recited in claim 15 of the present application. Applicants presume this may be because nowhere does Schlichte state this. Applicants do note, however, that discussion of an "oral" application of the marker formulation in Schlichte, or application of the formulation in the "mouth," appears at only three locations in Schlichte. First, in column 1, lines 7-9, Schlichte states that "[t]he present invention relates to a marker... applied either topically or orally." Second, in column 3, lines 22-23, Schlichte states that the "marker color will appear... in the mouth." And finally, in

column 3, lines 28-30, Schlichte states that the marker formulation can "be injected or given orally at a given day and appear at a later date or appear in a few hours." Applicants submit that none of these statements teach the oral administration and contact coloration of membranes as disclosed and claimed in the present application.

Applicants submit that even though Schlichte mentions "oral" and "mouth," there is no suggestion that such application leads to coloration and subsequent observation of mucous membranes of the oral and/or pharyngeal cavity. Nor is such coloration necessarily inherent, since Applicants submit that a marker formulation may be ingested and subsequently appear at a site distant to the oral and/or pharyngeal cavity. Also, such a marker formulation could appear in tissues of the mouth, as opposed to membranes. In fact, Applicants assert that a reading of the instances of "oral" and "mouth" in Schlichte clearly shows that Schlichte does not contemplate a coloration of the mucous or buccal membranes of the oral or pharyngeal cavities.

For example, while oral application is mentioned in a perfunctory manner in the "Field of the Invention" section of Schlichte, that oral application is described in slightly more detail in column 3 of the "Detailed Description." Applicants submit that a person of ordinary skill in the art reading column 3, lines 28-30, of Schlichte would take that disclosure to teach that the marker will appear (1) at a later time, and/or (2) at a location *other than* the administration site. For example, Schlichte states that the marker can be given "orally... and appear at a later date or appear in a few hours."

Thus, the oral application of the Schlichte marker formulation requires the passage of some amount of time for the marker to appear. Applicants submit that the reason for this time lapse is because, once orally ingested, the marker cannot rapidly appear in cutaneous or subcutaneous tissues since it must first be transported into those tissues. Such a time lapse is one of the drawbacks discussed in the "Background of the Invention" section of the present application, and which the invention of the present application overcomes.

Further, Schlichte discloses oral application in conjunction with a discussion of other application methods, such as injection. When a substance is injected, it is administered into the venous system, where it is then transported to a different location. Injection, therefore, is not a method used to mark a particular site where the injection itself occurs. Likewise, a marker formulation absorbed orally may then be transported and appear elsewhere. In view of the entire disclosure of Schlichte, Applicants submit that it is clear that this discussion of the marker formulation being injected or given orally only presumes a marker formulation which may then appear at a later time and/or at a location distant to the oral cavity, such as in the cutaneous or subcutaneous tissues of the hide of an animal, which a reading of the entire Schlichte reference will show is the thrust of the disclosure of Schlichte. Again, there is no teaching of a coloration of mucous and/or buccal membranes of the oral and/or pharyngeal cavity.

While column 3 of Schlichte does mention that the marker may appear "in the mouth," again, there is absolutely no disclosure that the marker appears in membranes of the oral and/or pharyngeal cavity, as is recited in claim 15. Applicants assert that a reading of the entire disclosure of Schlichte demonstrates that one skilled in the relevant art would read that the marker appears in cutaneous or subcutaneous tissues of the mouth. Thus, this disclosure in Schlichte does not teach an oral ingestion of a composition that colors the mucous or buccal membranes of the oral or pharyngeal cavity upon contact therewith.

In view of the above discussion, Applicants respectfully assert that the Schlichte '102 patent does not disclose each and every limitation of claim 15 of the present application and thus, neither does the Schlichte '102 patent disclose each and every limitation of dependent claims 2-14 and 16-27. Applicant thus respectfully requests a withdrawal of the rejection under 35 U.S.C. § 102.

Claim Rejections 35 U.S.C. §103:

1. **Schlichte/Pather**

The Examiner has rejected claims 21 and 22 under 35 U.S.C. § 103(a) as being unpatentable over the Schlichte '102 patent in view of U.S. Patent No. 6,200,604 (the Pather '604 patent). In particular, the Examiner states that the Pather '604 patent discloses carmine and FD&C dyes, and that it would have been obvious to use such

dyes in the marker composition of the Schlichte '102 patent for oral consumption, as taught by the Pather '604 patent. Applicants respectfully disagree.

With respect to the disclosure of the Schlichte '102 patent, as described above with respect to the § 102 rejection, Applicants respectfully submit that the Schlichte '102 patent only discloses a composition that is directed into cutaneous or subcutaneous tissues of a subject. The disclosure in the Schlichte '102 reference teaches only some time-consuming marking of such cutaneous or subcutaneous tissue, through invasive methods such as injection and implantation into the cutaneous or subcutaneous tissue. While Schlichte does reference "oral" application or the "mouth," nowhere is there a teaching in the Schlichte '102 reference of a marker which is active for coloration of a portion of a mucous membrane or buccal membrane of the oral/pharyngeal cavity. By contrast, the claims of the present application recite that contact coloration occurs in a mucous or buccal membrane of the oral and/or pharyngeal cavity. Applicants submit that such contact coloration, as recited in the claims of the present application, is clearly very different from the marking of the cutaneous or subcutaneous tissue as taught by the Schlichte '102 reference. Thus, even if one were to combine the dyes of Pather with the composition of Schlichte, Applicants submit that such a combination would not teach each and every limitation of the claims since the composition would be directed into cutaneous or subcutaneous tissues.

2. **Schlichte/Kell**

The Examiner has rejected claims 23-27 under 35 U.S.C. § 103(a) as being unpatentable over the Schlichte '102 patent in view of U.S. Patent No. 5,776,783 (the Kell '783 patent). In particular, the Examiner states that the Schlichte '102 patent discloses a composition having multiple medications, but does not disclose a marker associated with each medicament. The Examiner then asserts that the Kell '783 patent teaches a composition having multiple medications and separate markers associated with each medication in the formulation to monitor compliance with drug ingestion. The Examiner states that it therefore would have been obvious to provide multiple medications with markers associated with each medication in the composition of the Schlichte '102 patent wherein each marker has a unique coloring characteristic and residence time in the tissue to monitor compliance with drug ingestion, as taught by the Kell '783 patent. The Examiner finally asserts that the marker may be any color and is visible under a variety of lighting conditions, as taught by the Schlichte '102 patent. Applicants respectfully disagree.

With respect to the disclosure of the Schlichte '102 patent, as described above with respect to the § 102 rejection, Applicants respectfully submit that the Schlichte '102 patent only discloses a composition that is directed into cutaneous and subcutaneous tissues of a subject. The disclosure in the Schlichte '102 reference teaches only some marking of such cutaneous or subcutaneous tissue, through

invasive methods such as injection and implantation into the cutaneous or subcutaneous tissue. While Schlichte does minimally refer to "oral" application and the "mouth," nowhere is there a teaching in the Schlichte '102 reference of a marker which is active for coloring a portion of a mucous membrane or buccal membrane of the oral/pharyngeal cavity. By contrast, the newly added claims recite that contact coloration occurs in a mucous or buccal membrane of the oral and/or pharyngeal cavity. As above, Applicants submit that such contact coloration, as recited in the claims of the present application, is clearly very different from the marking of the cutaneous or subcutaneous tissue as taught by the Schlichte '102 reference. Thus, even if one were to combine the multiple markers of Kell with the composition of Schlichte, Applicants submit that such a combination would not teach each and every limitation of the claims, since the composition would be directed into cutaneous and subcutaneous tissues.

Further, Applicants assert that, were one to combine the Schlichte '102 patent and the Kell '783 patent, the combination does not teach the invention because the Kell '783 patent discloses a method of monitoring patient compliance with a medical regimen by testing the urine of a patient. Thus, Kell also does not teach the contact coloration of a mucous or buccal membrane. Additionally, analysis of urine is a process that is time consuming, intrusive, requires scheduling, and requires the presence of a trained technician. These are the very drawbacks of current monitoring methods, described in the "Background of the Invention" section of the present application, that

the present invention eliminates. In fact, urine analysis was one of the prior art monitoring methods that was discussed in the present application as wholly different than the compliance monitoring composition and method of the present invention. Even if one skilled in the art were to combine the teachings of Schlichte and Kell, they would not be directed to oral ingestion of a composition for contact coloration of a mucous or buccal membrane.

The present invention, by contrast, is rapid, simple, non-invasive, and inexpensive in that it is simply performed by observing a mucous or buccal membrane of the oral/pharyngeal cavity after oral ingestion for staining in order to determine compliance. Applicants thus respectfully assert that even if one were to attempt to detect the coloring agent of the Schlichte '102 patent, it could not be detected in the urine by the method disclosed by the Kell '783 patent, since such coloring agent would not be detectable in a patient's urine. Nor would such a coloring agent be visually observable in a patient's urine.

3. **Rittenburg/Schlichte**

The Examiner has rejected claims 1-7 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,068,981 (the Rittenburg '981 patent) in view of the Schlichte '102 patent. In particular, the Examiner states that the Rittenburg '981 patent discloses a method of monitoring compliance of a patient in a therapeutic or medication regimen wherein the method includes the steps of providing a therapeutic compound

and a marker that passes into tissue and detecting the marker in the tissue. The Examiner then further states that it would have been obvious to one of ordinary skill in the art to use a detectable compound that colors tissues in the mouth, as taught by the Schlichte '102 patent in the method of the Rittenburg '981 patent to provide visual evidence for gauging the application and time since application of the medicament. Applicants respectfully disagree.

With respect to the disclosure of the Schlichte '102 patent, as described above with respect to the § 102 rejection, Applicants respectfully submit that the Schlichte '102 patent only discloses marking of cutaneous or subcutaneous tissues in the subject. The disclosure in the Schlichte '102 reference teaches only some marking of such cutaneous or subcutaneous tissue, through invasive methods such as injection and implantation into the cutaneous or subcutaneous tissue. While Schlichte does minimally refer to "oral" application and the "mouth," nowhere is there a teaching in the Schlichte '102 reference of a marker which is active for contact coloration of a portion of a mucous membrane or buccal membrane of the oral/pharyngeal cavity.

By contrast, the newly added claims recite that contact coloration occurs in a mucous or buccal membrane of the oral and/or pharyngeal cavity. Applicants submit that such contact coloration, as recited in the claims of the present application, is clearly very different from the marking of the cutaneous or subcutaneous tissue through the very invasive methods taught by the Schlichte '102 reference. Further, the

Rittenburg '981 patent does not teach contact coloration of the mucous or buccal membrane of the oral and/or pharyngeal cavity, as claimed in the present application. Further, Rittenburg does not disclose visualization of the oral/pharyngeal cavity. Rather, Applicants submit that Rittenburg discloses a compound that passes into a system (such as bloodstream, excretory, or other fluid or tissue), and then detects a marker in a fluid or tissue sample taken from the subject. Again, these methods described in Rittenburg are also very invasive and time consuming. These are drawbacks with previous marking methods that were discussed in the "Background of the Invention" section of the present application, and which the invention of the present application overcomes. Additionally, in using these methods, even if one were to combine the method of Rittenburg with the composition of Schlichte, such a combination would not teach each and every limitation of claim 1. As such, any combination could not render claim 1 obvious, and thus Applicants respectfully request a withdrawal of the rejection of independent claim 1, and dependent claims 2-7.

4. **Rittenburg/Schlichte/Pather**

The Examiner has rejected claims 8 and 9 under 35 U.S.C. § 103(a) as being unpatentable over the Rittenburg '981 patent in view of the Schlichte '102 patent, and further in view of the Pather '604 patent. In particular, the Examiner states that it would have been obvious to one of ordinary skill in the art to use carmine dyes or FD&C

dyes, as disclosed in the Pather '604 patent, in the method of the combination of the Rittenburg '981 and Schlichte '102 patents. Applicants respectfully disagree.

In particular, as described above with respect to the rejection of claims 1-7, the combination of the Schlichte '102 patent and Rittenburg '981 patent do not disclose all the limitations of independent claim 1 of the present invention. In particular, the Schlichte '102 patent discloses use of its compositions only in cutaneous or subcutaneous tissues, not contact coloration or observation in mucous or buccal membranes. Nor does the Rittenburg '981 patent disclose observation in the mucous or buccal membranes. Thus, any combination of the Schlichte '102 patent disclosure with the method described in the Rittenburg patent would not disclose each and every limitation of the present application, since the combination of those two patents would not disclose contact coloration in a mucous or buccal membrane of the oral and/or pharyngeal cavity of the patient. Thus, since independent claim 1 would not be rendered obvious, Applicants respectfully submit that neither would dependent claims 8 and 9 be rendered obvious in further view of the Pather '604 patent.

5. Rittenburg/Kell/Schlichte

The Examiner has rejected claims 10-14 under 35 U.S.C. § 103(a) as being unpatentable over the Rittenburg '981 patent in view of the Kell '783 patent further in view of the Schlichte '102 patent. In particular, the Examiner states that it would have been obvious to provide a composition with multiple medicaments in the

combination of Rittenburg and Kell, wherein each maker has unique coloring characteristics, residence time, and lighting conditions, as taught by Schlichte. Applicants respectfully disagree.

With respect to the disclosure of the Schlichte '102 patent, as described above with respect to the § 102 rejection, Applicants respectfully submit that the Schlichte '102 patent only discloses use of the composition as directed into cutaneous or subcutaneous tissues. Thus, it does not disclose contact coloration in the mucous or buccal membranes. Neither do Rittenburg or Kell disclose contact coloration of the mucous or buccal membranes. Further, the method of Rittenburg discloses detecting marker in a body fluid or tissue that has been collected, while Kell discloses detecting a marker in a urine sample. By contrast, the newly added claims recite that contact coloration occurs and is visualized in a mucous or buccal membrane of the oral and/or pharyngeal cavity. Thus, Applicants submit that even if one were to combine the disclosures of Rittenburg, Kell, and Schlichte, such a combination would not teach each and every limitation of the claims.

Further, each of the Schlichte, Kell, and Rittenburg references describe invasive and time-consuming methods that the present application overcomes by the claimed composition and method. Thus, one of ordinary skill of the art, even were they to combine those references, would not be directed to the simple and rapid method of the present application. As described above, the Schlichte '102 patent discloses a

composition which may mark only a cutaneous or subcutaneous tissue, and the Kell '783 patent discloses a method of monitoring patient compliance with a medical regimen by testing the urine of a patient. Applicants thus respectfully assert that even if one were to attempt to detect the coloring agent of the Schlichte '102 patent, it could not be detected in the urine by the method disclosed by the Kell '783 patent, since such coloring agent would not be detectable in a patient's urine. Nor would such a coloring agent be visually observable in a patient's urine. In fact, as described above, these are the very invasive and time consuming drawbacks, that the invention of the present invention overcomes. Applicants further assert that the combination of Rittenburg with Schlichte would fail for the same reasons as the combinations of Kell and Schlichte.

Conclusion:

For the foregoing reasons, Applicants submit that all claims are patentable and a Notice of Allowance is respectfully requested.

The Commissioner is hereby authorized to charge deposit account no. 23-3000 in the amount of $770.00 for the fee set forth in 37 C.F.R. §1.17(e). No additional fee is believed due with this submission. However, if any additional fees or surcharges are deemed due, please charge same or credit any overpayment to deposit account no. 23-3000.

The Examiner is invited to contact the undersigned attorney with any questions or remaining issues.

Respectfully submitted,

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